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FINAL REPORT
OF
THE WOBURN ADVISORY PANEL
TO
THE MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH
JUNE, 1985

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The panel was privileged to hear directly, at a public meeting, of the experiences, perceptions and concerns of Woburn residents. Nothing else could have conveyed so meaningfully both the adversities that this community has faced and the courage and discipline with which its people have met those adversities.

Summary

The people of Woburn have experienced more than their share of certain diseases, the most serious being childhood leukemia. The present report is prepared by the Advisory Panel in response to the understandable concerns raised within the community and among relevant local, State and Federal officials and agencies by this elevated disease experience.

There have been 19 incident cases of childhood leukemia in Woburn children over the past 15 years, when only 6 would have been expected. There have also been reports of excessive rates for other diseases, such as, certain birth defects and adult cancers, but for these the evidence is weak. The Massachusetts Department of Health and the Centers for Disease Control have documented the excess of childhood leukemia in a series of reports, and have also carried out a case-control study. In a collaboration between members of the Biostatistics Department, Harvard School of Public Health, and the residents of Woburn, another study was done; this implicated drinking water drawn from two wells known to have been contaminated with chemicals, as being associated with childhood leukemia and selected birth defects. It was explicitly not the charge of the Advisory Panel to pass judgment on these various studies but all were made available to the panel members and were carefully studied.

The distribution of childhood leukemia constitutes a cluster, that is, an unusual concentration of cases in time and place. Clusters of childhood leukemia and cancer have been reported before: 101 have been investigated in



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the U.S. by the Centers for Disease Control since 1963 with no cause discovered for any of them. Typically, such excess frequencies are not sustained and leave no clue as to the reason that they occurred. The possibility cannot be discounted that the Woburn cluster will disappear in the same way as have the others. Nevertheless, we have four reasons for suggesting that the circumstances of the Woburn cluster call for further studies.

First and foremost, the raised frequency of childhood leukemia in Woburn has not yet disappeared. The persistent excess mandates watchfulness. The emphasis of our recommendations is on such watchfulness over the next few years, which should be on the one hand rigorous and systematic, on the other as undisturbing as possible to the ongoing life of the community.

Second, scientific advances have clarified the role of genetic processes and viruses in rare forms of childhood cancer in humans and in animals. This new knowledge now permits fresh approaches to the investigation of some cases of childhood leukemia. One might, for instance, speculate that a viral agent "caused" some of the previously reported clusters in children, but that newer techniques were not available to discover it. The present opportunity for a sophisticated search for a cause should not be lost.

Third, a putative cause, exposure to contaminated water has been proposed and investigated in this community. While the strength of the supporting evidence is debatable, there is no basis for ruling out this possibility at the present time. This provides a third reason for continuing studies.

Fourth, evidence of the unusually pervasive presence of multiple

environmental toxins resulting from the community's history of intensive industrialization over the past century suggests the desirability of health and environmental monitoring. These four considerations have guided the panel in emphasizing the value of further studies. Our recommendations will deal in turn with:

1. The epidemiological features of the cluster in Woburn; clues that the epidemiologist could pursue to determine the unique nature of the Woburn experience in comparison with other reported clusters; evidence that might point to the waning or persistence of the cluster and what the attendant strategies of action should be.

2. A closer investigation of incident cases of childhood leukemia and heir families in the continuing search for etiologic clues.

3. The needed integrated evaluation of the quality of the physical environment (air, soil and water) covering the past, present and future. Although no specific hypotheses are being proposed, our purpose is to ensure that the maintenance of environmental standards becomes more systematic, regular and visible.

4. The panel has responded in the fourth section of this report to a theme raised several times in community meetings, for Woburn to be regarded as a model or exemplary community in terms of public health watchfulness for adverse health effects, especially those that might relate to the physical environment. Several of the recommendations in this report speak directly to this theme. It is in this spirit that we have proposed an infant and child health monitoring program be set up in Woburn. Also in this context, we propose broadening the focus from childhood leukemia to other (less well substantiated) reported excesses, specifically in selected birth defects and kidney cancer.

An active education program is proposed as part of the recommendation involving agency personnel as well as residents. This would facilitate the understanding and participation of the community, its physicians and hospitals, etc. with reference to testing, data collection and the dissemination and interpretation of test results. It would also ensure that the program meets the needs of the community, giving staff an awareness and appreciation of the residents' responses and concerns.

5. Lastly, the several recommendations flowing from this report include the need for an implementation plan, the assignment of agency and community responsibilities, emphasis on co-ordination between the agencies, a two-way flow of information and action between the agencies, and the community. This in turn, suggests the desirability of assigning a State or Federal agency staff person to these tasks on a regular basis.

RECOMMENDATIONS

1. Epidemiological Studies of the Cluster of Childhood Leukemia

1.1 It is recommended that a complete list of incident cases of leukemia in children (up to the age of 15 years) residing in Woburn at the time of diagnosis be compiled. The list should cover the period 1965 to 1984. For each child, these items should be recorded:

Date of birth

Sex of child

Place of birth (if in Woburn, preferably precise address)

Later places of residence and dates

Age and place of diagnosis

Type of cell involved in the disease

Response to treatment(s)

If deceased, date and cause

1.2 This list should be updated, in detail, over the succeeding five years. It should be supplemented as far as possible with information on incident cases in children previously residing in Woburn but identified elsewhere.

If these actions are taken, it becomes possible to develop a decision strategy based on the number of new cases that might arise over an observation period. Specific suggestions of how to interpret the waning, waxing or persistence of an excess are set out in Appendix I.

1.3 The cluster of Woburn cases should be compared systematically, for the characteristics of the condition as set out in 1.1., with cases culled from registers or other sources on the one hand, and with cases studied in earlier clusters on the others. This may reveal any obvious and unique features of the Woburn cluster, or of all clusters.

1.4 Regarding the hypothesis that contamination of wells G and H "caused" the cluster of cases, the panel weighed the evidence and found itself left with uncertainty. However, it was noted that in the event that the excess of cases of childhood leukemia continues, the hypothesis would be weakened; in the event that the frequency wanes, the hypothesis cannot be ruled out, but it is by no means established.

2. Studies of Etiology

2.1 Any new findings or clues that emerge from studies of the physical environment should be rigorously tested against the health outcomes.

2.2 A systematic protocol for investigation of all new cases should be followed. An outline is proposed in Appendix II.

2.3 Encouragement should be given to researchers to characterize fully in the laboratory the cell type and the chromosomal aberrations present in existing and incident cases of childhood leukemia from Woburn. The excess of a rare subtype, for instance, would add to the view that the cluster indeed represents, perhaps in part, a response to a common cause.

2.4 Encouragement should be given to competent scientists to consider a possible viral etiology in the Woburn cluster of childhood leukemia.

A puzzling feature of the clusters reported in Woburn and elsewhere is that susceptibility seems to be confined to young children.^{FN} This is not a feature of those few physical or chemical exposures known to cause leukemia or cancer in humans. In animals, an excess of cancer in the young does occur with certain leukemia viruses, although in the only virus known to induce leukemia in humans, the young are not especially susceptible. Since the cluster of leukemia in Woburn is occurring only in children, there is a striking similarity to the

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Adult proportional incidence ratios (PIR) are 100 for males and 77 for females indicating that the incidence for both males and females is either at or below what would have been expected (Massachusetts Cancer Registry, 1982 and 1983 Data.)

animal leukemogenic virus models. A prudent course of action, therefore, is to initiate investigations into a possible viral etiology for the cases in Woburn. Tissue material and serum might be banked, for instance, for use in future studies.

The fuller justification of this recommendation is set out in Appendix II.

3. Studies of the Physical Environment

3.1 It is recommended that an integrated review be undertaken of present, past and likely future circumstances with regard to impact on the soil, water and air environments.

The review should include both public and private developments (industrial and municipal waste management) and should be done in a temporal and spatial manner by constructing maps and providing overlays to give a sequential picture of historical and contemporary events. Existing data bases may provide the foundation for this work.

3.2 For the future: an integrated monitoring system is recommended. The entire Woburn area seems vulnerable because of potential "saturation" with wastes. Therefore, not only wells G and H, but other well water and surface waters must be monitored. (Details are set out in Appendix III).

3.3 Comprehensive air sampling, indoor and outdoor, is recommended. Disposal of organic solvents may serve as a source of atmospheric contamination when uncovered through industrial and community developments. Suspected dumpsites, municipal and industrial, require such testing.

3.4 A target list of likely hazardous contaminants should be generated, based on the results of the above studies; future monitoring would then focus on these. The presence of chromium, cadmium and arsenic should be especially evaluated in this connection.

3.5 Water from various sources, including the recently closed wells G and H, should be tested for mutagenicity.

3.6 Co-ordination between agencies and a clear assignment of responsibilities is required for effective monitoring of the physical environment.

4. Health Surveillance in Woburn: A Model Community

4.1 It is recommended that a health surveillance system should be developed in Woburn which would be complementary to the studies of the physical environment described under 3, above. Selected health outcomes as well as environmental elements would be monitored in an ongoing way for a period of five years. Such a system would involve active community participation.

This recommendation is based on two considerations. The first relates to the uncertainty regarding present and future trends in several health outcomes in Woburn, which warrants a non-invasive watchfulness, especially of serious childhood disorders. The second relates to the historic circumstances of the Woburn community which has left residents acutely aware of the need for special surveillance measures and hence receptive to appropriate innovations that should enhance the health of their community.

4.2 A program is recommended that would watch over the frequency of serious childhood conditions, at birth, during infancy, and at school entry.

In implementing such a program, existing data bases should first be examined, adapted, and as far as possible co-ordinated to provide source material for the needed frequencies. New systems should only be created when existing ones are deficient. The most accessible endpoints should be selected for study in the first place; birthweight, gender (for sex ratio), fetal death rate, early, late and post neonatal infant mortality; death from selected causes; and malformations as entered on birth certificates and death certificates. Hospital records, especially those that are computerized, provide another convenient source (for instance, for pre-eclamptic toxemia; congenital cardiac anomalies; limb and facial defects). Hospital discharge summaries and pediatric clinic records may be used to identify congenital anomalies identified within the first year of life but not at birth. Laboratories may provide information on chromosomal anomalies and blood dyscrasias. The Massachusetts Cancer Registry is an essential source.

4.3 Consideration might be given at some later date to supplementing these existing sources with additional endpoints, or with better characterization of some data already collected. Examples are suggested in the Appendix; thus neuro-developmental delay, noted at school-entry, would be additional; standardized listing of defects at birth by trained observers would greatly improve on existing procedures.

4.4 Certain descriptive material would be maintained for children with selected serious disorders (leukemia; congenital malformations) and for their families, if they are residents in Woburn. The purpose would not be to test a specific hypothesis, but to pioneer the health monitoring which we consider

to be a desirable routine for modern industrialized communities. No unnecessary procedures would be involved, but additional laboratory tests could be included as well as fuller and more systematic records than are usual on pregnancy, infancy and family.

4.5 Descriptive material would also be maintained on a small number of "well" children and their families comparable to those in the groups described above. This method of documenting in a routine way the experiences of an unaffected child and family at the same time as it is done for an affected one, has been used as part of an ongoing routine of monitoring in Sweden and Finland for a decade, but not yet, to our knowledge, in a U.S. community. It makes it immediately possible to explore an unusual excess of cases, should such occur, with comparative material.

4.6 If these or similar procedures should be established, it is essential that the endpoints under study be regularly assessed. Appropriate comparisons will be needed. One source of comparative data is the experience in a current year compared to a prior; another is the experience in neighboring or comparable communities.

4.7 Monitoring of the physical environment, including assessment of possible human exposure to lead, may be seen as one component of the plan for a model community. Children should be screened for lead exposure, as a routine pediatric health procedure (although there is no evidence of an excess of raised lead levels in Woburn). A simple, rapid and inexpensive method is to examine a drop of blood for erythrocyte porphyrin (EP), from every child who has blood drawn for other health purposes. Children with raised levels should be evaluated for possible lead toxicity and/or iron deficiencies and

treated as required. For those with elevated lead levels, the source of exposure should be sought and removed.

4.8 Continued community involvement and leadership are essential in this enterprise. This will ensure informed participation in the surveillance program. It might serve to dispel certain misapprehensions: for instance, that effects of present environmental exposures would influence subsequent generations of births, an extremely unlikely outcome. It would also provide a forum for decision making, for example, on the issue of whether the benefits of a sister chromatid exchange (SCE) screening program are outweighed by the uncertainties in interpretation that would be associated with such a program (see Appendix IV).

4.9 Agency personnel should join residents and interested professionals in the development of this program. This should ensure the appropriateness and acceptability of the program, to the community.

5. Implementation

5.1 A first task is to generate an implementation plan, based on those elements of this report that are accepted as desirable and feasible.

5.2 A next step is to assign responsibility for those aspects of the plan that are to be implemented. Presumably the assignee would be a nominee of the Massachusetts Department of Public Health.

5.3 A strong recommendation is for co-ordination between the agencies (DOE, EPA) that must share responsibility with MDPH for the activities mentioned in the report. A mechanism is needed for arranging and maintaining this co-ordination.

5.4 Communication and meaningful participation must be facilitated between the residents of Woburn, the MDPH, and the other responsible agencies. Communication is seen as a two-way process including consultation and exchange of information and opinions. Every attempt should be made to reach the community through several different levels, including official bodies (the Mayor), professional groups (especially medical practitioners, health workers and perhaps teachers), existing organizations concerned with health and the environment, organizations like PTAs and church groups, and the local press.

5.5 In order to minimize duplication and overlap, a mechanism is needed to establish a clearinghouse of environmental and health related data that are collected by individual agencies on a routine or sporadic basis. The clearing house should co-ordinate and catalogue data from all the agencies, thereby making a wide range of material available to interested parties.

APPENDICES

I.

STRATEGIES FOR DECISION MAKING

For how long should a state of watchfulness be maintained? In one sense a modest alerting system as described in the report should be permanently in place. However, regarding the cluster of childhood leukemia, the duration of high level alertness and the decisions that need to be taken at each juncture need serious consideration.

Several logical alternative outcomes and a priori criteria for decision making in conjunction with these outcomes are outlined:

A. In the event of attenuation of the cluster of childhood leukemia.

1. Should no additional case occur within the next five years (1985-1989) the panel suggests that the level of monitoring with respect to childhood leukemia be reduced from "exceptional" to routine. The monitoring programs listed in part 4 of the panel statement should still continue, because they serve the community in other ways and stand as good public health practices.

2. If, in the subsequent five years (1990-1994) the rate of childhood leukemia or other indication of interest falls into the background rate, the exceptional programs need not be reinstated. Monitoring programs listed in part 4 may be reviewed and continued in whole or in part.

B. In the event of one incident case of childhood leukemia in five years:

1. What should be done if the case arises in the G-H area and involves a child conceived after the wells were closed? In this eventuality, the hypothesis that the G-H wells are the source of childhood leukemia in Woburn

should be considered of doubtful validity. This outcome should trigger activities in two directions:

a. Extensive data should be collected on all prior and incident cases of childhood leukemia, not only with respect to possible exposure to biological and chemical contaminants but also with respect to life-styles; e.g., socio-economic standing, professions of the employed adults, play habits of the child, etc.

b. Standard statistical analyses should be employed which would permit an exploration of competing hypotheses. Such analyses may require a small population survey to develop comparative data bases.

2. If the case arises outside the G-H area

We cannot, in this case, reject the "G-H hypothesis". An important contributory factor may be water of the "G-H type" which does not come directly from the G-H wells; i.e., the contaminants of the G-H wells may be moving into other wells or other wells may have become similarly but independently contaminated from some other source. Therefore, an exploratory study could be done, using the Harvard study as a starting point (perhaps corrected in respect of a revised model of water flow) for designing and rapidly implementing data collection and analysis. However, the analysis again should permit the evaluation of alternative hypotheses.

C. In the event that new cases continue to appear in Woburn at present or increased level (that is, there is no apparent attenuation of the cluster).

Should there be a clear continuation of the cluster (e.g., 3 cases in any two year period), then the situation calls for a renewed and vigorous

effort to identify a cause. The analysis of present data and the collection of new data must be pursued. The lines of inquiry would be determined at that time from an investigation, for example, of the biological and social characteristics of the cases and from the studies of the physical environment. A population study to obtain comparative data will also be needed. It is suggested that some of the techniques, developed and used by World Health Organization (WHO) for collecting information rapidly and inexpensively in such an environment, be exploited. It is further suggested that the Health Department prepare protocols and sampling frames in the near future, in order that a tentative survey could be accomplished in a timely fashion should it be necessary.

II.

STUDIES OF ETIOLOGY

Procedures to Monitor Incident Cases

Appropriately, a Childhood Leukemia Registry has already been created for children born in Woburn since 1965. No special effort is needed to ascertain new cases because they will quickly come to notice in consequence of the great public concern about this cancer.

The clinical presentation, laboratory findings and course of the 20 cases that have occurred should be evaluated for unusual features in common which may indicate that the Woburn cluster is not due to chance.

The subtyping of new and existing leukemia cases is crucial, because the same subtype in most cases would suggest an etiology in common. Subtyping involves classification according to cell-surface markers and cytogenetic abnormalities in a particular leukemia. Specimens for such study should be obtained before treatment of new cases, if at all possible, or when already treated patients are in remission. These and other specimens (serum and lymphocytes--nascent and Epstein Barr Virus-transformed) should be stored frozen, so they are available for study when appropriate procedures are developed in the future. For studies of oncogenes, normal tissue (e.g., skin fibroblasts or possibly lymphocytes in remission) will be needed for comparison with tumor cells from the same patient. Consideration should be given to collecting specimens from the immediate family.

As each new case is ascertained, personal and family histories should be obtained. Special attention should be given to exposures to known leukemogens

(ionizing radiation, benzene and marrow-depressant drugs), as well as the occurrence of cancer in persons or pets in the same household.

Even though there is no evidence for a viral etiology related to the increased occurrence of cases of acute lymphoblastic leukemia (ALL) in children in Woburn nor has animal virus-leukemia ever been shown to be transmitted to man, still there are examples of virus-related leukemia in animals. Clusters of lymphoid leukemias have been caused by oncogenic viruses in several animal species, and chickens, mice, cats, cows and gibbon apes have contagious leukemia viruses. Except for the adult T-cell leukemias (ATL) that have been caused by the only known leukemia virus in humans (HTLV-I), animal leukemogenic viruses induce more leukemia in young animals when compared to adult animals. Many adult animals presently infected with leukemia viruses remain as healthy carriers for long periods of time or develop non-neoplastic diseases rather than leukemia.

In further support of investigation of a possible viral etiology, in both the cow and cat leukemia animal models viral-induced virus "non-producer" leukemias occur frequently. Cows with leukemia do not replicate bovine leukemia virus (BLV) in vivo, probably because of the production of anti-BLV antibodies that are present in such cattle. However, BLV can be isolated from leukemic cells grown in culture, free from antibody, after only 3 days. Similarly, 30% of FeLV-induced leukemia of pet cats are virus non-producer tumors. However, latent FeLV can be reactivated from bone marrow cells but not from the leukemic cells. Both of these animal models of viral-induced but virus negative leukemias may be relevant to the study of a possible viral etiology of childhood acutelymphocytic leukemia (ALL) in Woburn. Some retroviral researchers suggest that other human retroviruses may

exist and, if so, the Woburn cluster of ALL may be a very valuable source of investigative material.

Consideration could be given to the collection and storage of tissue material and serum relating to cases of childhood leukemia involved in the Woburn cluster, thereby facilitating investigations at a later stage.

III.

MONITORING THE PHYSICAL ENVIRONMENT

The entire Woburn area deserves attention because of potential "saturation" with wastes. Therefore, an integrated monitoring approach is warranted. We suggest that all media be examined, not only emphasizing wells G and H, but other well and surface waters. It is likely that wherever there was an industrial activity in the past, such as a tannery, the ground was contaminated. With subsequent leaching, this contamination most likely was translocated. Hence, sediments in receiving streams and other surface waters should be examined.

Results of sediment testing may ultimately justify selected biological monitoring, and may suggest migration routes of materials (contaminants from outside the area of concern may be migrating into the area). The sediments may well store heavy metal concentrations and possibly organic compounds. Hence, the sediments are an important transport mechanism and reservoir for contaminants. Its contact with the overlying waters provides continuing exposure to the water resource. Moreover, this combination of water and sediment may encourage interphase transport and volatilization. This again emphasizes the necessity of recognizing the exchange between the three primary environmental phases, i.e., soil, water and air, in any effective monitoring program.

IV.

A MODEL COMMUNITY: MONITORING HEALTH OUTCOMES

An innovative community health strategy, as proposed in Section 4 above and further expanded here, requires in the first place a context in which all participating individuals and groups (residents, health professionals, agency staff) may learn from each other. Thus, scientific, administrative, economic, and ethical issues could be involved, and the "fit" between the proposed investigation and the community response must be considered. While no precise mechanisms for this broad but essential educational exercise are set down here, we would see the responsibility for its initiation to lie with the person(s) assigned to the role of implementation and co-ordination.

The following specific procedures are suggested as exemplifying the kind of health outcome monitoring that might be initiated in Woburn.

A. Reproductive Outcome Monitoring Program

Preliminary studies suggested that a possible increase in some birth defects may have occurred in the Woburn population. While the panel neither accepts nor rejects this suggestion, it recommends that existing data bases (such as the Birth Defects Monitoring Program of Atlanta, Georgia maintained by the Centers for Disease Control) and the literature should be evaluated to provide additional insights into whether the incidence of certain adverse outcomes in Woburn is truly elevated. (For example, the question was raised by the Harvard study whether the incidence of eye anomalies was increased beyond the expected level, but comparisons with other population studies do not suggest an excess. The frequency of strabismus in the NIH Collaborative Perinatal Study, 1.87% is not significantly higher than the 1.5% reported

in the Harvard study, in the G-H Woburn area. Perhaps the rate of 0.15%, elsewhere in Woburn is due to under-ascertainment.)

The panel recommends the establishment of a reproductive outcome monitoring program which would promptly detect any differences that might arise in the incidence of selected reproductive and perinatal outcomes within the Woburn population.

In developing a reproductive outcome monitoring program the Panel recommends the following general guidelines:

- The area selected should be large enough to provide 5000 births per year. Thus, the area would encompass Woburn (which has about 400 births per year) and neighboring towns.

- The monitored area should be population based (using US Census units) to permit the calculation of incidence and prevalence rates.

- In constructing the area to be monitored, some account should be taken of the number of hospitals in which deliveries occur, in order to maximize the efficiency of data collection.

- The time to collect, analyze and report data within the monitoring system should be minimized so as to maintain the sensitivity of the system to currently existing environmental risks.

- The system should be flexible enough to permit additional specialized studies of specific reproductive outcomes.

The reproductive outcomes to be studied should include:

1. Structural, chromosomal and genetic congenital malformations
(excluding documented birth injuries)

2. Birth weight
3. Gender (for sex ratio)
4. Perinatal, late neonatal and infant mortality
5. Pre-eclampsia

B. Monitoring the Incidence of Minor Defects or Developmental Delay

1. We propose for consideration that voluntary examinations for children in the first year of life be offered to residents of Woburn and to one other community which could serve as a control. Referral could be made by local pediatricians, health care personnel or parents. The physical exam, to be carried out by an appropriately trained clinician, would comprise a complete dysmorphic evaluation using a standardized check list for anomalies (e.g., as used by Dr. Lewis Holmes). A screening developmental assessment (for example, the Bailey) could also be given. Counseling and referral would be given as appropriate to families. The risk of "detection bias" requires that such a program also be undertaken in a control population.

2. The panel further recommends that MDPH review the data on health and development already being collected at the time of school entry, for its suitability as a neuro-developmental screen for problems in Woburn school children. If appropriate to the purpose, the frequency and type of problems observed in Woburn school children may be compared to expected values, derived from comparable communities.

These examinations, in the first year of life and at school entry, might elucidate specific causes and diagnoses not detectable at birth. Affected families should be given the pertinent information about these conditions, including etiology and prognosis where known, and a list of recommended referral specialists in the area.

C. Selection of Controls for Children with Selected Health Outcomes

The case control approach has been applied to the study on the Woburn cluster of childhood leukemias identified prior to 1980. By careful matching of cases with concurrent controls, some opportunity is afforded to identify possible risk factors and describe how incident cases compare with or differ from matched controls. The continuation of this approach would seem to be desirable in the interests of gathering the broadest possible data base and identifying possible causative factors specific to Woburn. We suggest in the report that this approach would be suitable, not only for childhood leukemia but also for other serious childhood disorders.

A general logic is proposed for the selection of controls in a Woburn based case-control study. Two lines of reasoning apply in this selection process. One is that the excess childhood leukemias arise in Woburn as a consequence of some characteristic(s) that distinguish this community generally from its neighbors. The second line is that the leukemias are geographically specific within certain parts of Woburn. A suitable control in the first instance would be a child in a neighboring town with a similar history of industrialization. The corresponding control for the second instance is a well child within Woburn residing in a different geographic area (or in some other fashion appropriately distinguished) from the previously identified cases.

In practice, multiple controls (say, four), chosen and matched in various ways, would be optimal. The cost would be slight because all the disorders of interest are very rare.

D. Sister Chromatid Exchange Studies (SCE)

The panel considered whether SCE monitoring was appropriate or necessary for selected groups of the Woburn population. While it was not felt to be timely to engage in SCE monitoring at this time, the Panel believes the feasibility of SCE monitoring should be further explored taking into account the following points:

1. Experts in SCE and environmental monitoring are available in the Boston area.

2. Community anxieties, which may be raised by SCE screening, need to be addressed. In particular, any SCE testing of individuals should have informed consent. The use of SCE tests as monitoring measures in the community could cause increased anxiety and loss of credibility if results were announced that showed an increased level of SCEs - especially if the community had no prior knowledge of the study.

3. Before the initiation of any screening program, detailed planning should be in place as to the actions that might be advisable in the event that elevated rates of SCEs were to be detected in Woburn.

4. The absence of any health effects attributable to SCE is recognized.

E. Early Pregnancy Studies

The feasibility of studying early pregnancy loss among a volunteer group of women planning to become pregnant, might be considered. Two series are being studied by research groups (one in Research Triangle, and one in New York) and Woburn women could be compared with these, and perhaps also with a further control series in the vicinity.



